

addition to the compounds wherein Y is aryl. The description as a whole is sufficient to evidence possession of the claimed genus.

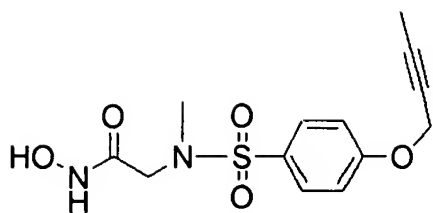
Looking at the basic structure of the compounds of the present invention, the positions of R₁, R₅, R₈, R₉, R₁₀, R₁₁, R₁₂ and Y include both aryl and heteroaryl among the members of each group. Many of the disclosed heteroaryls, such as benzothiophene, pyrrole, isoquinoline, quinoline, isoindol and the like, have been exemplified and shown to possess TACE inhibiting activity. Within the scope of this invention, it is clear that Y can be a heteroaryl based on the interchangeability of aryls and heteroaryls in other representative compounds of this invention. One of ordinary skill in the art would appreciate that there is a correlation between structure and function in the chemical art and the specification shows a correlation between structure and function that would yield the desired biological properties. Hence, the written description complies with the statutory requirement because it can depend upon the correlation for sufficiency.

The Examiner also rejected Claims 1, 2 and 5-7 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement for reasons set forth in the Office action on pages 3 and 4. Applicants respectfully traverse this rejection for the following reasons.

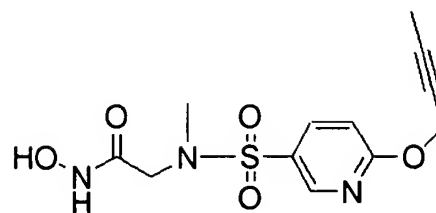
The test of enablement is whether the specification contains an adequate disclosure of the claimed invention to enable the ordinary practitioner to make and use the invention without undue experimentation. As the Examiner kindly points out, there are many factors to be considered when determining whether the disclosure satisfies the enablement requirement. In light of those factors, Applicants assert that the ordinary chemist would easily be able to make and use any of the claimed heteroaryl compounds without undue effort. Consequently, the specification satisfies the test of enablement.

Contrary to the Examiner's belief, Applicants do not believe that the claims are extremely broad. Rather, the claims recite a reasonable number of well-suited, defined substituents that can be placed on the core structure.

In terms of the level of predictability in the art, Applicants have based the structure-activity correlation and the interchangeability of aryl and heteroaryl in the Y position upon their own prior published and patented work in other series of TACE inhibitors. For example, similar aryl (phenyl) and heteroaryl (pyridyl) compounds, which have been described in U.S. Patent No. 6,225,311 B1, have been shown to possess reasonably close TACE inhibiting activity as follows:



TACE IC_{50} = 7 nM



TACE IC_{50} = 29 nM

Thus, the predictability in the art is known due to the art that has TACE inhibiting aryl and heteroaryl compounds that work.

The generic claims provide direction to the chemist to appreciate that the illustrated Y as phenyl may readily be substituted by other aryls and the heteroaryl. Based on the extensive teaching and examples of key positions throughout the compound structure (R_1 , Y, R_8 , R_{10} , R_{12} , *etc.*) that can provide a heteroaryl substituent (benzothiophene, pyrrole, isoquinoline and the like), it is reasonable to assume that Y can also be heteroaryl without adversely affecting the integrity and activity of the compounds of the invention.

It has been well established that working examples are not a statutory requirement (*Ex parte Nardi and Simier*, 229 U.S.P.Q. 79 (B.P.A.I. 1986)). Thus, the absence of an example in the instant specification wherein Y is heteroaryl is not fatal to Applicants' position.

More importantly, it is plain to see that one of ordinary skill in the chemical art would be able to prepare all of the heteroaryl derivatives of the claimed invention without undue effort. The process of making these compounds would be clear and routine to the ordinary chemist based on the guidelines illustrated in the application for many representative compounds in light of current chemical literature such as, for example, the online chemical databases, standard textbooks on organic synthesis and other widely available resources (see, for example, the numerous compounds that can be prepared via the basic steps of Examples 13 and 23). Thus, the quantity of experimentation needed to make and use the present invention would merely be routine.

In view of the foregoing remarks and the proffered evidence, Applicants respectfully request that the rejection of Claims 1, 2 and 5-7 under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description and enablement requirements be withdrawn and that the application be held allowable.

Accordingly, this application is in condition for an allowance. Favorable treatment is respectfully solicited.

Respectfully submitted,

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